Refine Search

Search Results -

Term	Documents
TRANSCRIPTION$3	0
TRANSCRIPTION	73882
TRANSCRIPTIONA	7
TRANSCRIPTIONAAL	1
TRANSCRIPTIONAI	2
TRANSCRIPTIONAL	36716
TRANSCRIPTIONALL	1
TRANSCRIPTIONALY	4
TRANSCRIPTIONAL]	2
TRANSCRIPTIONAND	2
TRANSCRIPTIONARE	1
(L4 AND TRANSCRIPTION$3).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	16

There are more results than shown above. Click here to view the entire set.

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
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EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L5

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Monday, May 03, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set

DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=ADJ

L5	L4 and transcription$3	16	L5
L4	L3 and androgen	16	L4
L3	L2 or l1	27	L3
L2	receptor tr4	17	L2
L1	tr4 orphan receptor	13	L1

END OF SEARCH HISTORY

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FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> SS TR4 ORPHAN RECEPTOR# OR RECEPTOR TR4
L1          162 TR4 ORPHAN RECEPTOR# OR RECEPTOR TR4

=> S L1 AND ANDROGEN3
L2            0 L1 AND ANDROGEN3

=> S L1 AND ANDROGEN#
L3           17 L1 AND ANDROGEN#

=> S L3 AND TRANSCRIPTION?
L4            9 L3 AND TRANSCRIPTION?

=> S L4 NAD DISEASE
MISSING OPERATOR L4 NAD
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> S L4 AND DISEASE
L5            2 L4 AND DISEASE

=> DUP REM L4
PROCESSING COMPLETED FOR L4
L6            7 DUP REM L4 (2 DUPLICATES REMOVED)

=> DUP REM L5
PROCESSING COMPLETED FOR L5
L7            1 DUP REM L5 (1 DUPLICATE REMOVED)

=> D IBIB ABS L5

L5   ANSWER 1 OF 2  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER:     2001-381186 [40]    WPIDS
DOC. NO. NON-CPI:     N2001-279520
DOC. NO. CPI:         C2001-116707
TITLE:                Method for screening compound, for use in treatment of
                        ***androgen***  - and estrogen-related   ***diseases***
                      , comprises testing compound to determine its effects on
                      nuclear receptor-mediated   ***transcriptional***
                      activity.
DERWENT CLASS:        B04 S03
INVENTOR(S):          CHANG, C
PATENT ASSIGNEE(S):   (UYRP) UNIV ROCHESTER; (CHAN-I) CHANG C
COUNTRY COUNT:        94
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK      LA   PG
     ---------------------------------------------
     WO 2001035101    A2 20010517 (200140)* EN   37
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
            LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
            SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001017639    A  20010606 (200152)
     US 2003235860    A1 20031225 (200408)

APPLICATION DETAILS:

     PATENT NO      KIND                  APPLICATION          DATE
     ------------------------------------------------------------
     WO 2001035101  A2                    WO 2000-US31189      20001113
     AU 2001017639  A                     AU 2001-17639        20001113
     US 2003235860  A1 Provisional        US 1999-165300P      19991112
                       CIP of             US 2000-711585       20001113
                                          US 2003-366811       20030213

FILING DETAILS:
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PATENT NO	KIND	PATENT NO
AU 2001017639	A Based on	WO 2001035101

PRIORITY APPLN. INFO: US 1999-165300P 19991112; US 2000-711585 20001113; US 2003-366811 20030213

AN 2001-381186 [40] WPIDS

AB WO 200135101 A UPAB: 20010719

NOVELTY - A method for screening a compound for use in the treatment of ***androgen*** -related ***diseases*** comprises testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity and observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.

DETAILED DESCRIPTION - A method for screening a compound for use in the treatment of ***androgen*** -related ***diseases*** comprises:

(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from TR2 orphan receptor, the ***TR4*** ***orphan*** ***receptor*** and the RXR receptor; and

(b) observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.

INDEPENDENT CLAIMS are also included for:

(1) a method for screening a compound for use in treatment of estrogen-related ***diseases*** comprising:

(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from TR2 orphan receptor, the ***TR4*** ***orphan*** ***receptor*** and the RXR receptor; and

(b) observing the effect of the compound on the level of estrogen receptor-initiated ***transcription*** in the test; and

(2) a method for modulating the sensitivity of a cell to a sex hormone comprising the step of stimulating in the cell the abundance (sic) of a nuclear receptor selected from the groups consisting of TR2 orphan receptor, the ***TR4*** ***orphan*** ***receptor*** and the RXR receptor

(3) a method for modulating the ***androgen*** receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate TR2 orphan receptor level or ***TR4*** ***orphan*** ***receptor*** level in the cell;

(4) a method for down regulating ***androgen*** receptor-mediated transactivation activity in a cell comprising introducing TR2 receptor orphan ligand binding domain or ***TR4*** ***orphan*** ***receptor*** ligand binding domain into the cell;

(5) a method for modulating estrogen receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate TR2 orphan receptor level or ***TR4*** ***orphan*** ***receptor*** level in the cell;

(6) a method for down regulating TR2 orphan receptor-mediated transactivation activity in a cell by introducing estrogen receptor ligand binding domain into the cell;

(7) a method for screening a compound for treating ***androgen*** receptor-related ***diseases*** by exposing cells to the compound and determining the effect of the compound on TR2 or ***TR4*** ***orphan*** ***receptor*** signaling pathway in the cells; and

(8) a method for screening a compound for treating estrogen receptor-related ***diseases*** by exposing cells to the compound and determining the effect of the compound on TR2 orphan receptor signaling pathway in those cells.

ACTIVITY - Cytotoxic.

MECHANISM OF ACTION - Suppressor of transactivation activity of nuclear receptors. A reporter assay was performed to study the potential effects of AR-TR4 heterodimer formation on transactivation. Full-length AR and TR4 in eukaryotic expression vectors (pSG5AR and pCMXTR4) were co-transfected with a CAT reporter containing a TR4-response element (DR4-TK-CAT). More specifically, reporter plasmids (DR4-CAT and CNTFR-15-LUC) (500 ng) were co-transfected with pCMX-TR4 and increasing amounts of pCMV-AR (200, 600 and 1200 ng), pSG5GR (1200 ng) or pSG5PR (1200 ng) using the SuperFect transfection kit. It was found that the CAT activity induced by pCMXTR4 could be repressed significantly in a dose-dependent manner by co-transfection of pSG5AR in the absence or presence of DHT. The repression of TR4 transactivation was AR specific, as other activated steroid receptors such as GR or PR had no suppressive effects. Similar effects were observed when DR4-TK-CAT receptor was replaced with D R1-CNTFR-15-LUC, another response element.

USE - The invention is useful in the control or treatment of ***diseases*** or clinical conditions such as hepatitis, hepatoma and hair loss that may relate to TR4 transactivation activity. It is also useful in the treatment of ER-related ***diseases*** . In general, modulating nuclear receptor transactivating activity has proved successful in treating ***diseases*** that are related to such nuclear transactivating activity. For example, certain types of breast cancer can be controlled by blocking the estrogen receptor transactivation using the antiestrogen tamoxifen.

ADVANTAGE - Understanding how nuclear receptor activity such as that of ***androgen*** receptor, estrogen ***receptor*** , ***TR4*** and TR2 is regulated and how these receptors interact with each other will advance the understanding of many human ***diseases*** and clinical conditions. Consequently, new treatment options, new drug screening methods and new diagnostic tools will emerge. ***Androgen*** receptor (AR) and TR4 receptor heterodimerize with each other, as do estrogen receptor (ER) and TR2 orphan receptor. Such heterodimer formation represses the transactivation activity of both receptors of each heterodimer. This allows TR4-related ***diseases*** to be controlled or cured through modulating AR levels, as well as drugs to be screened for TR4-related ***diseases*** , by testing their effects on AR level. Similarly the invention makes it possible to screen for drugs for ER-related ***diseases*** by testing a compound's effect on TR2 level. It was also found that the RXR receptor can also suppress transactivation of the AR receptor through co-suppression by an allied nuclear receptor. Dwg.0/10

=> D IBIB ABS L6 1-7

L6 ANSWER 1 OF 7 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2004:355790 SCISEARCH
THE GENUINE ARTICLE: 810JX
TITLE: ***Androgen*** receptor coregulators in prostate cancer: Mechanisms and clinical implications
AUTHOR: Rahman M; Miyamoto H; Chang C S (Reprint)
CORPORATE SOURCE: Univ Rochester, Ctr Med, George Whipple Lab Canc Res, Dept Biochem, 601 Elmwood Ave, Rochester, NY 14642 USA (Reprint); Univ Rochester, Ctr Med, George Whipple Lab Canc Res, Dept Biochem, Rochester, NY 14642 USA; Univ Rochester, Ctr Med, George Whipple Lab Canc Res, Dept Pathol, Rochester, NY 14642 USA; Univ Rochester, Ctr Med, George Whipple Lab Canc Res, Dept Urol, Rochester, NY 14642 USA; Univ Rochester, Ctr Med, George Whipple Lab Canc Res, Dept Radiat Oncol, Rochester, NY 14642 USA; Univ Rochester, Ctr Med, George Whipple Lab Canc Res, Ctr Canc, Rochester, NY 14642 USA
COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL CANCER RESEARCH, (1 APR 2004) Vol. 10, No. 7, pp. 2208-2219.
Publisher: AMER ASSOC CANCER RESEARCH, 615 CHESTNUT ST, 17TH FLOOR, PHILADELPHIA, PA 19106-4404 USA.
ISSN: 1078-0432.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 151

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1007725 CAPLUS
DOCUMENT NUMBER: 140:53957
TITLE: Compositions and methods related to interactions between ***androgen*** receptor, estrogen receptor, and testicular orphan nuclear receptors
INVENTOR(S): Chang, Chawnshang
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of U.S. Ser. No. 711,585.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003235860	A1	20031225	US 2003-366811	20030213
PRIORITY APPLN. INFO.:			US 1999-165300P P	19991112

US 2000-711585 A2 20001113

AB Disclosed are compns. and methods related to TR2 (testicular orphan nuclear receptor 2), TR4 (testicular orphan nuclear receptor 4), ***androgen*** receptor, and estrogen receptor and the interactions between these proteins. Specifically claimed are compns. comprising a fragment of TR2, wherein the compn. interacts with ER, such that ER ***transcriptional*** activity is decreased. Methods of identifying an inhibitor of an interaction between ER and TR2 and of identifying inhibitors of ER ***transcription*** activity are also claimed. Addnl. claimed are methods of inhibiting TR4 ***transcription*** activity comprising administering a compn. that binds TR4, wherein the compn. is AR, AR fragment, AR variant, a mol. that competitively competes with TR4 for AR binding, or a combination thereof. A method of identifying an inhibitor of an interaction between AR and TR4 is also claimed.

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:146192 CAPLUS
DOCUMENT NUMBER: 138:332617
TITLE: Identification of a novel testicular orphan receptor-4 (TR4)-associated protein as repressor for the selective suppression of TR4-mediated transactivation
AUTHOR(S): Yang, Yue; Wang, Xin; Dong, Tiefei; Kim, Eungseok; Lin, Wen-Jye; Chang, Chawnshang
CORPORATE SOURCE: George Whipple Laboratory for Cancer Research Departments of Pathology and Cancer Center, Radiation Oncology, Urology, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Journal of Biological Chemistry (2003), 278(9), 7709-7717
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although many co-activators have been identified for various nuclear receptors, relatively fewer co-repressors have been isolated and characterized. Here we report the identification of a novel testicular orphan nuclear receptor-4 (TR4)-assocd. protein (TRA16) that is mainly localized in the nucleus of cells as a repressor to suppress TR4-mediated transactivation. The suppression of TR4-mediated transactivation is selective because TRA16 shows only a slight influence on the transactivation of ***androgen*** receptor, glucocorticoid receptor, and progesterone receptor. Sequence anal. shows that TRA16 is a novel gene with 139 amino acids in an open reading frame with a mol. mass of 16 kDa, which did not match any published gene sequences. Mammalian two-hybrid system and co-immunopptn. assays both demonstrate that TRA16 can interact strongly with TR4. The electrophoretic mobility shift assay suggests that TRA16 may suppress TR4-mediated transactivation via decreased binding between the TR4 protein and the TR4 response element on the target gene(s). Furthermore, TRA16 can also block the interaction between TR4 and TR4 ligand-binding domain through interacting with TR4-DNA-binding and ligand-binding domains. These unique suppression mechanisms suggest that TRA16 may function as a novel repressor to selectively suppress the TR4-mediated transactivation.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 7 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:360462 SCISEARCH
THE GENUINE ARTICLE: 545EH
TITLE: Modulation of estrogen receptor-mediated transactivation by orphan ***receptor*** ***TR4*** in MCF-7 cells
AUTHOR: Shyr C R; Hu Y C; Kim E; Chang C S (Reprint)
CORPORATE SOURCE: Univ Rochester, Med Ctr, Dept Pathol, George Whipple Lab Canc Res, Rochester, NY 14642 USA (Reprint); Univ Rochester, Med Ctr, Dept Urol, George Whipple Lab Canc Res, Rochester, NY 14642 USA; Univ Rochester, Med Ctr, Dept Radiat Oncol, George Whipple Lab Canc Res, Rochester, NY 14642 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (26 APR 2002) Vol. 277, No. 17, pp. 14622-14628.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal

LANGUAGE: English
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The human testicular orphan receptor 4 (TR4) is a member of the nuclear receptor superfamily that shows a broad tissue distribution with higher expression in the nervous system and male reproductive tract. TR4 functions as a ***transcriptional*** modulator that controls various target genes via binding to the DNA hormone response elements. Here we report that instead of direct binding to hormone response elements for gene regulation, TR4 can also go through direct protein-protein interaction to repress estrogen receptor (ER)-mediated transactivation. Electrophoretic mobility shift and glutathione S-transferase pull-down assays clearly demonstrate that the direct interaction between TR4 and ER will inhibit the homodimerization of ER and interrupt/prevent ER binding to the estrogen response element. The consequence of these events may then result in the suppression of ER target genes, such as cyclin D1 and pS2 and inhibition of ER-mediated cell proliferation in the MCF-7 cells stably transfected with TR4. Together, our results showing that TR4 can suppress ER function via protein-protein interaction not only represent a unique cross-talk signaling pathway in the nuclear receptor superfamily, it may also provide us with a new strategy to modulate ER function in the breast cancer cells.

L6 ANSWER 5 OF 7 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 1
ACCESSION NUMBER: 2001-381186 [40] WPIDS
DOC. NO. NON-CPI: N2001-279520
DOC. NO. CPI: C2001-116707
TITLE: Method for screening compound, for use in treatment of ***androgen*** - and estrogen-related diseases, comprises testing compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity.
DERWENT CLASS: B04 S03
INVENTOR(S): CHANG, C
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER; (CHAN-I) CHANG C
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001035101	A2	20010517	(200140)*	EN	37
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001017639	A	20010606	(200152)		
US 2003235860	A1	20031225	(200408)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001035101	A2	WO 2000-US31189	20001113
AU 2001017639	A	AU 2001-17639	20001113
US 2003235860	A1 Provisional	US 1999-165300P	19991112
	CIP of	US 2000-711585	20001113
		US 2003-366811	20030213

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001017639	A	Based on	WO 2001035101

PRIORITY APPLN. INFO: US 1999-165300P 19991112; US 2000-711585 20001113; US 2003-366811 20030213
AN 2001-381186 [40] WPIDS
AB WO 200135101 A UPAB: 20010719
NOVELTY - A method for screening a compound for use in the treatment of ***androgen*** -related diseases comprises testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity and observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.
DETAILED DESCRIPTION - A method for screening a compound for use in

the treatment of ***androgen*** -related diseases comprises:

(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from TR2 orphan receptor, the ***TR4*** ***orphan*** ***receptor*** and the RXR receptor; and

(b) observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.

INDEPENDENT CLAIMS are also included for:

(1) a method for screening a compound for use in treatment of estrogen-related diseases comprising:

(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from TR2 orphan receptor, the ***TR4*** ***orphan*** ***receptor*** and the RXR receptor; and

(b) observing the effect of the compound on the level of estrogen receptor-initiated ***transcription*** in the test; and

(2) a method for modulating the sensitivity of a cell to a sex hormone comprising the step of stimulating in the cell the abundance (sic) of a nuclear receptor selected from the groups consisting of TR2 orphan receptor, the ***TR4*** ***orphan*** ***receptor*** and the RXR receptor

(3) a method for modulating the ***androgen*** receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate TR2 orphan receptor level or ***TR4*** ***orphan*** ***receptor*** level in the cell;

(4) a method for down regulating ***androgen*** receptor-mediated transactivation activity in a cell comprising introducing TR2 receptor orphan ligand binding domain or ***TR4*** ***orphan*** ***receptor*** ligand binding domain into the cell;

(5) a method for modulating estrogen receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate TR2 orphan receptor level or ***TR4*** ***orphan*** ***receptor*** level in the cell;

(6) a method for down regulating TR2 orphan receptor-mediated transactivation activity in a cell by introducing estrogen receptor ligand binding domain into the cell;

(7) a method for screening a compound for treating ***androgen*** receptor-related diseases by exposing cells to the compound and determining the effect of the compound on TR2 or ***TR4*** ***orphan*** ***receptor*** signaling pathway in the cells; and

(8) a method for screening a compound for treating estrogen receptor-related diseases by exposing cells to the compound and determining the effect of the compound on TR2 orphan receptor signaling pathway in those cells.

ACTIVITY - Cytotoxic.

MECHANISM OF ACTION - Suppressor of transactivation activity of nuclear receptors. A reporter assay was performed to study the potential effects of AR-TR4 heterodimer formation on transactivation. Full-length AR and TR4 in eukaryotic expression vectors (pSG5AR and pCMXTR4) were co-transfected with a CAT reporter containing a TR4-response element (DR4-TK-CAT). More specifically, reporter plasmids (DR4-CAT and CNTFR-15-LUC) (500 ng) were co-transfected with pCMX-TR4 and increasing amounts of pCMV-AR (200, 600 and 1200 ng), pSG5GR (1200 ng) or pSG5PR (1200 ng) using the SuperFect transfection kit. It was found that the CAT activity induced by pCMXTR4 could be repressed significantly in a dose-dependent manner by co-transfection of pSG5AR in the absence or presence of DHT. The repression of TR4 transactivation was AR specific, as other activated steroid receptors such as GR or PR had no suppressive effects. Similar effects were observed when DR4-TK-CAT receptor was replaced with D R1-CNTFR-15-LUC, another response element.

USE - The invention is useful in the control or treatment of diseases or clinical conditions such as hepatitis, hepatoma and hair loss that may relate to TR4 transactivation activity. It is also useful in the treatment of ER-related diseases. In general, modulating nuclear receptor transactivating activity has proved successful in treating diseases that are related to such nuclear transactivating activity. For example, certain types of breast cancer can be controlled by blocking the estrogen receptor transactivation using the antiestrogen tamoxifen.

ADVANTAGE - Understanding how nuclear receptor activity such as that of ***androgen*** receptor, estrogen ***receptor*** , ***TR4*** and TR2 is regulated and how these receptors interact with each other will advance the understanding of many human diseases and clinical conditions. Consequently, new treatment options, new drug screening methods and new diagnostic tools will emerge. ***Androgen*** receptor (AR) and TR4 receptor heterodimerize with each other, as do estrogen receptor (ER) and TR2 orphan receptor. Such heterodimer formation represses the transactivation activity of both receptors of each heterodimer. This

allows TR4-related diseases to be controlled or cured through modulating AR levels, as well as drugs to be screened for TR4-related diseases, by testing their effects on AR level. Similarly the invention makes it possible to screen for drugs for ER-related diseases by testing a compound's effect on TR2 level. It was also found that the RXR receptor can also suppress transactivation of the AR receptor through co-suppression by an allied nuclear receptor.
Dwg.0/10

L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:11220 CAPLUS
DOCUMENT NUMBER: 132:146813
TITLE: Convergence of two repressors through heterodimer formation of ***androgen*** receptor and testicular orphan receptor-4: a unique signaling pathway in the steroid receptor superfamily
AUTHOR(S): Lee, Yi-Fen; Shyr, Chih-Rong; Thin, Tin Htwe; Lin, Wen-Jye; Chang, Chawnshang
CORPORATE SOURCE: George Whipple Lab for Cancer Research, Departments of Pathology, Urology, and Radiation Oncology, and The Cancer Center, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(26), 14724-14729
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ***androgen*** receptor (AR) binds to ***androgen*** response elements and regulates target genes via a mechanism involving coregulators. The AR can interact with the testicular orphan receptor-4 (TR4) and function as a repressor to down-regulate the TR4 target genes by preventing the TR4 binding to its target DNA. Interestingly, the heterodimerization of AR and TR4 also allows TR4 to repress AR target gene expression. Simultaneous exposure to both receptors therefore could result in bidirectional suppression of their target genes. Together, these data demonstrate that the coupling of two different receptors, through the heterodimerization of AR and TR4, is a unique signaling pathway in the steroid receptor superfamily, which may facilitate further understanding of the complicated ***androgen*** action in prostate cancer or libido.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999094280 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9879671
TITLE: Thyroid hormone direct repeat 4 response element is a positive regulatory element for the human TR2 orphan receptor, a member of steroid receptor superfamily.
AUTHOR: Chang C; Pan H J
CORPORATE SOURCE: Department of Pathology, University of Rochester, NY 14642, USA.
SOURCE: Molecular and cellular biochemistry, (1998 Dec) 189 (1-2) 195-200.
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990402
Last Updated on STN: 19990402
Entered Medline: 19990323
AB We demonstrate that TR2 orphan receptor (TR2) may induce transactivation activities via an AGGTCA-like-direct-repeat-4 consensus thyroid hormone response element (DR4-TRE) system. TR2 showed a slightly greater binding affinity than thyroid hormone receptor alpha1 (TR alpha1)/retinoid X receptor alpha (RXR alpha) heterodimer with Kds 0.5 nM and 2.3 nM, respectively. These receptors, TR2 and TR alpha1/RXR alpha heterodimer, competed with each other on binding to limited amounts of DR4-TRE. TR2 canceled the suppression effect of unliganded-TR alpha1 on CAT reporter activity in a dose-dependent fashion. Estrogen receptor (ER) and 2P2 (a mutated TR2 with P box sequence of ***androgen*** receptor) failed not only to bind to DR4-TRE but also to recover this inhibitory effect of unliganded TRalpha1. However, when T3 was supplemented, estradiol-ER competed for a full CAT activity while TR2 showed an additive effect on

the ***transcriptional*** activation. These results indicate that DNA binding is essential for TR2 to take action and fully functional liganded TR alpha1 may rely on common factors shared with ER but not TR2.

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FILE 'MEDLINE'

FILE 'JAPIO' E
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
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L1          97 TR2 ORPHAN RECEPTOR#

=> S RECEPTOR TR2
L2         235 RECEPTOR TR2

=> S L1 OR L2
L3         276 L1 OR L2

=> S L3 AND ANDROGEN#
L4          35 L3 AND ANDROGEN#

=> S L4 AND TRANSCRIPTION?
L5          24 L4 AND TRANSCRIPTION?

=> L5 AND DISEASE#
L6           3 L5 AND DISEASE#

=> DUP REM L6
PROCESSING COMPLETED FOR L6
L7           2 DUP REM L6 (1 DUPLICATE REMOVED)

=> D IBIB ABS L7 1-2

L7   ANSWER 1 OF 2  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 1
ACCESSION NUMBER:     2001-381186 [40]   WPIDS
DOC. NO. NON-CPI:     N2001-279520
DOC. NO. CPI:         C2001-116707
TITLE:                Method for screening compound, for use in treatment of
                        ***androgen***  - and estrogen-related   ***diseases***
                      , comprises testing compound to determine its effects on
                      nuclear receptor-mediated   ***transcriptional***
                      activity.
DERWENT CLASS:        B04 S03
INVENTOR(S):          CHANG, C
PATENT ASSIGNEE(S):   (UYRP) UNIV ROCHESTER; (CHAN-I) CHANG C
COUNTRY COUNT:        94
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK      LA   PG
     ----------------------------------------------
     WO 2001035101    A2 20010517 (200140)* EN   37
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
            LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
            SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001017639    A  20010606 (200152)
     US 2003235860    A1 20031225 (200408)

APPLICATION DETAILS:

     PATENT NO      KIND                  APPLICATION          DATE
     ------------------------------------------------------------------
     WO 2001035101  A2                    WO 2000-US31189      20001113
     AU 2001017639  A                     AU 2001-17639        20001113
     US 2003235860  A1 Provisional        US 1999-165300P      19991112
                       CIP of             US 2000-711585       20001113
                                          US 2003-366811       20030213

FILING DETAILS:

     PATENT NO        KIND                  PATENT NO
     ----------------------------------------------
     AU 2001017639    A  Based on           WO 2001035101

PRIORITY APPLN. INFO: US 1999-165300P      19991112; US
```

2000-711585 20001113; US
2003-366811 20030213

AN 2001-381186 [40] WPIDS

AB WO 200135101 A UPAB: 20010719

NOVELTY - A method for screening a compound for use in the treatment of ***androgen*** -related ***diseases*** comprises testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity and observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.

DETAILED DESCRIPTION - A method for screening a compound for use in the treatment of ***androgen*** -related ***diseases*** comprises:

(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor; and

(b) observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.

INDEPENDENT CLAIMS are also included for:

(1) a method for screening a compound for use in treatment of estrogen-related ***diseases*** comprising:

(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor; and

(b) observing the effect of the compound on the level of estrogen receptor-initiated ***transcription*** in the test; and

(2) a method for modulating the sensitivity of a cell to a sex hormone comprising the step of stimulating in the cell the abundance (sic) of a nuclear receptor selected from the groups consisting of ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor

(3) a method for modulating the ***androgen*** receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate ***TR2*** ***orphan*** ***receptor*** level or TR4 orphan receptor level in the cell;

(4) a method for down regulating ***androgen*** receptor-mediated transactivation activity in a cell comprising introducing TR2 receptor orphan ligand binding domain or TR4 orphan receptor ligand binding domain into the cell;

(5) a method for modulating estrogen receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate ***TR2*** ***orphan*** ***receptor*** level or TR4 orphan receptor level in the cell;

(6) a method for down regulating ***TR2*** ***orphan*** ***receptor*** -mediated transactivation activity in a cell by introducing estrogen receptor ligand binding domain into the cell;

(7) a method for screening a compound for treating ***androgen*** receptor-related ***diseases*** by exposing cells to the compound and determining the effect of the compound on TR2 or TR4 orphan receptor signaling pathway in the cells; and

(8) a method for screening a compound for treating estrogen receptor-related ***diseases*** by exposing cells to the compound and determining the effect of the compound on ***TR2*** ***orphan*** ***receptor*** signaling pathway in those cells.

ACTIVITY - Cytotoxic.

MECHANISM OF ACTION - Suppressor of transactivation activity of nuclear receptors. A reporter assay was performed to study the potential effects of AR-TR4 heterodimer formation on transactivation. Full-length AR and TR4 in eukaryotic expression vectors (pSG5AR and pCMXTR4) were co-transfected with a CAT reporter containing a TR4-response element (DR4-TK-CAT). More specifically, reporter plasmids (DR4-CAT and CNTFR-15-LUC) (500 ng) were co-transfected with pCMX-TR4 and increasing amounts of pCMV-AR (200, 600 and 1200 ng), pSG5GR (1200 ng) or pSG5PR (1200 ng) using the SuperFect transfection kit. It was found that the CAT activity induced by pCMXTR4 could be repressed significantly in a dose-dependent manner by co-transfection of pSG5AR in the absence or presence of DHT. The repression of TR4 transactivation was AR specific, as other activated steroid receptors such as GR or PR had no suppressive effects. Similar effects were observed when DR4-TK-CAT receptor was replaced with D R1-CNTFR-15-LUC, another response element.

USE - The invention is useful in the control or treatment of ***diseases*** or clinical conditions such as hepatitis, hepatoma and hair loss that may relate to TR4 transactivation activity. It is also useful in the treatment of ER-related ***diseases*** . In general, modulating nuclear receptor transactivating activity has proved successful in treating ***diseases*** that are related to such nuclear

transactivating activity. For example, certain types of breast cancer can be controlled by blocking the estrogen receptor transactivation using the antiestrogen tamoxifen.

ADVANTAGE - Understanding how nuclear receptor activity such as that of ***androgen*** receptor, estrogen receptor, TR4 and TR2 is regulated and how these receptors interact with each other will advance the understanding of many human ***diseases*** and clinical conditions. Consequently, new treatment options, new drug screening methods and new diagnostic tools will emerge. ***Androgen*** receptor (AR) and TR4 receptor heterodimerize with each other, as do estrogen receptor (ER) and ***TR2*** ***orphan*** ***receptor*** . Such heterodimer formation represses the transactivation activity of both receptors of each heterodimer. This allows TR4-related ***diseases*** to be controlled or cured through modulating AR levels, as well as drugs to be screened for TR4-related ***diseases*** , by testing their effects on AR level. Similarly the invention makes it possible to screen for drugs for ER-related ***diseases*** by testing a compound's effect on TR2 level. It was also found that the RXR receptor can also suppress transactivation of the AR receptor through co-suppression by an allied nuclear receptor.

Dwg.0/10

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:529246 CAPLUS
DOCUMENT NUMBER: 131:168353
TITLE: Identification of loci involved in accelerated wound healing and the development of new wound healing promoters
INVENTOR(S): Heber-Katz, Ellen
PATENT ASSIGNEE(S): The Wistar Institute, USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941364	A2	19990819	WO 1999-US2962	19990212
WO 9941364	A3	19991223		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319700	AA	19990819	CA 1999-2319700	19990212
AU 9926720	A1	19990830	AU 1999-26720	19990212
EP 1053309	A1	20001122	EP 1999-906924	19990212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002503460	T2	20020205	JP 2000-531545	19990212
US 2003037345	A1	20030220	US 1999-249155	19990212
US 6538173	B2	20030325		
US 2003229911	A1	20031211	US 2002-314322	20021209

PRIORITY APPLN. INFO.:

US 1998-74737P	A2	19980213
US 1998-97937P	A2	19980826
US 1998-102051P	A2	19980928
US 1999-249155	A3	19990212
WO 1999-US2962	W	19990212

AB Genes that quant. improve the efficiency and effectiveness of wound healing in mice are identified. Wound healing is assayed by measuring the time taken for a 2 mm hole punched into the ear to heal. The genes or gene products may be useful in the development of new wound healing promoters, including agents for treatment of central and peripheral nerve wounds. Wound healing in the rapidly healing mouse line MRL was studied. In comparison to the C57BL/6 line, the MRL mice showed more extensive vascularization around wounds with rapid development of sebaceous glands and hair follicles and the unexpected appearance of adipocytes. These mice also showed improved healing of damage to the optic and sciatic nerve after crushing, and of the spinal cord after complete transection. Using the difference in wound healing behavior of the two lines, genetic polymorphisms assocd. with QTLs affecting wound healing were identified.

The accelerated healing of the MRL line was lost with aging, and this appeared to be as a result of T-cell actions. Macrophages from the MRL accelerated wound healing in control mice.

=> D HIS

FILE 'MEDLINE, JAPIO, BIOSIS, SCISEARCH, WPIDS, CAPLUS, EMBASE' ENTERED

L1 97 S TR2 ORPHAN RECEPTOR#
L2 235 S RECEPTOR TR2
L3 276 S L1 OR L2
L4 35 S L3 AND ANDROGEN#
L5 24 S L4 AND TRANSCRIPTION?
L6 3 L5 AND DISEASE#
L7 2 DUP REM L6 (1 DUPLICATE REMOVED)

=> DUP REM L5
PROCESSING COMPLETED FOR L5
L8 11 DUP REM L5 (13 DUPLICATES REMOVED)

=> S IBIB ABS L8 1-11
MISSING OPERATOR ABS L8
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> D IBIB ABS L8 1-11

L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:856090 CAPLUS
DOCUMENT NUMBER: 139:346360
TITLE: Method for obtaining the binding affinities of a peptide library to a protein
INVENTOR(S): Guy, Kip R.; Moore, Jamie M. R.; Geistlinger, Timothy R.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089662	A1	20031030	WO 2003-US11766	20030415

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004005636	A1	20040108	US 2003-414583	20030415

PRIORITY APPLN. INFO.: US 2002-372952P P 20020415
OTHER SOURCE(S): MARPAT 139:346360
AB The present invention provides a method for measuring the binding of a peptide library to a target protein, both in the presence and absence of a ligand, or other activation modifier. The peptide library is chosen from known binding partners of the target protein, or members of the family to which it belongs. The members of the peptide library include a conserved interaction motif that permits them to bind to the target protein or its family. Individual peptides from the peptide library and the target protein are contacted with one another and a binding affinity measured. The binding affinities across the library are treated as a 'fingerprint'. The method is preferably applied to a library of co-regulatory peptides that bind to a nuclear hormone receptor. The present invention further comprises the peptide library, and a compn. comprising a member of the peptide library in contact with the target protein.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1007725 CAPLUS
DOCUMENT NUMBER: 140:53957
TITLE: Compositions and methods related to interactions between ***androgen*** receptor, estrogen receptor, and testicular orphan nuclear receptors
INVENTOR(S): Chang, Chawnshang
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of U.S. Ser. No. 711,585.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003235860	A1	20031225	US 2003-366811	20030213

PRIORITY APPLN. INFO.: US 1999-165300P P 19991112
US 2000-711585 A2 20001113

AB Disclosed are compns. and methods related to TR2 (testicular orphan nuclear receptor 2), TR4 (testicular orphan nuclear receptor 4), ***androgen*** receptor, and estrogen receptor and the interactions between these proteins. Specifically claimed are compns. comprising a fragment of TR2, wherein the compn. interacts with ER, such that ER ***transcriptional*** activity is decreased. Methods of identifying an inhibitor of an interaction between ER and TR2 and of identifying inhibitors of ER ***transcription*** activity are also claimed. Addnl. claimed are methods of inhibiting TR4 ***transcription*** activity comprising administering a compn. that binds TR4, wherein the compn. is AR, AR fragment, AR variant, a mol. that competitively competes with TR4 for AR binding, or a combination thereof. A method of identifying an inhibitor of an interaction between AR and TR4 is also claimed.

L8 ANSWER 3 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:775118 SCISEARCH
THE GENUINE ARTICLE: 592WD
TITLE: Suppression of estrogen receptor-mediated ***transcription*** and cell growth by interaction with ***TR2*** ***orphan*** ***receptor***
AUTHOR: Hu Y C; Shyr C R; Che W Y; Mu X M; Kim E; Chang C (Reprint)
CORPORATE SOURCE: Univ Rochester, Med Ctr, George Whipple Lab Canc Res, Dept Pathol, 601 Elmwood Ave, Box 626, Rochester, NY 14642 USA (Reprint); Univ Rochester, Med Ctr, George Whipple Lab Canc Res, Dept Pathol, Rochester, NY 14642 USA; Univ Rochester, Med Ctr, George Whipple Lab Canc Res, Dept Urol, Rochester, NY 14642 USA; Univ Rochester, Med Ctr, Ctr Canc, Rochester, NY 14642 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (13 SEP 2002) Vol. 277, No. 37, pp. 33571-33579.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 62

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ***transcriptional*** activity of the estrogen receptor (ER) is known to be highly modulated by the character and amount of coregulator proteins present in the cells. ***TR2*** ***orphan*** ***receptor*** (***TR2***), a member of the nuclear receptor superfamily without identified ligands, is found to be expressed in the breast cancer cell lines and to function as a repressor to suppress ER-mediated ***transcriptional*** activity. Utilizing an interaction blocker, ER-6 (amino acids 312-340), responsible for TR2 interaction, the suppression of ER by TR2 could be reversed, suggesting that this suppression is conferred by the direct protein-protein interaction. Administration of antisense TR2, resulting in an enhancement of ER ***transcriptional*** activity in MCF7 cells, indicates that endogenous TR2 normally suppresses ER-mediated signaling. To gain insights into the molecular mechanism by which TR2 suppresses ER, we found that TR2 could interrupt ER DNA binding via formation of an ER-TR2 heterodimer that disrupted the ER homodimerization. The suppression of ER

transcription by TR2 consequently caused the inhibition of estrogen-induced cell growth and G(1)/S transition in estrogen-dependent breast cancer cells. Taken together in addition to the potential roles in spermatogenesis and neurogenesis, our data provide a novel biological function of TR2 that may exert an important repressor in regulating ER activity in mammary glands.

L8 ANSWER 4 OF 11 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 1
ACCESSION NUMBER: 2001-381186 [40] WPIDS
DOC. NO. NON-CPI: N2001-279520
DOC. NO. CPI: C2001-116707
TITLE: Method for screening compound, for use in treatment of ***androgen*** - and estrogen-related diseases, comprises testing compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity.
DERWENT CLASS: B04 S03
INVENTOR(S): CHANG, C
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER; (CHAN-I) CHANG C
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001035101	A2	20010517	(200140)*	EN	37
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001017639	A	20010606	(200152)		
US 2003235860	A1	20031225	(200408)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001035101	A2	WO 2000-US31189	20001113
AU 2001017639	A	AU 2001-17639	20001113
US 2003235860	A1 Provisional	US 1999-165300P	19991112
	CIP of	US 2000-711585	20001113
		US 2003-366811	20030213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001017639	A Based on	WO 2001035101

PRIORITY APPLN. INFO: US 1999-165300P 19991112; US 2000-711585 20001113; US 2003-366811 20030213
AN 2001-381186 [40] WPIDS
AB WO 200135101 A UPAB: 20010719
NOVELTY - A method for screening a compound for use in the treatment of ***androgen*** -related diseases comprises testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity and observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.
DETAILED DESCRIPTION - A method for screening a compound for use in the treatment of ***androgen*** -related diseases comprises:
(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor; and
(b) observing the effect of the compound on the level of ***androgen*** receptor-initiated ***transcription*** in the test.
INDEPENDENT CLAIMS are also included for:
(1) a method for screening a compound for use in treatment of estrogen-related diseases comprising:
(a) testing the compound to determine its effects on nuclear receptor-mediated ***transcriptional*** activity, the activity being mediated by a nuclear receptor selected from ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor; and
(b) observing the effect of the compound on the level of estrogen receptor-initiated ***transcription*** in the test; and

(2) a method for modulating the sensitivity of a cell to a sex hormone comprising the step of stimulating in the cell the abundance (sic) of a nuclear receptor selected from the groups consisting of ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor

(3) a method for modulating the ***androgen*** receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate ***TR2*** ***orphan*** ***receptor*** level or TR4 orphan receptor level in the cell;

(4) a method for down regulating ***androgen*** receptor-mediated transactivation activity in a cell comprising introducing TR2 receptor orphan ligand binding domain or TR4 orphan receptor ligand binding domain into the cell;

(5) a method for modulating estrogen receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate ***TR2*** ***orphan*** ***receptor*** level or TR4 orphan receptor level in the cell;

(6) a method for down regulating ***TR2*** ***orphan*** ***receptor*** -mediated transactivation activity in a cell by introducing estrogen receptor ligand binding domain into the cell;

(7) a method for screening a compound for treating ***androgen*** receptor-related diseases by exposing cells to the compound and determining the effect of the compound on TR2 or TR4 orphan receptor signaling pathway in the cells; and

(8) a method for screening a compound for treating estrogen receptor-related diseases by exposing cells to the compound and determining the effect of the compound on ***TR2*** ***orphan*** ***receptor*** signaling pathway in those cells.

ACTIVITY - Cytotoxic.

MECHANISM OF ACTION - Suppressor of transactivation activity of nuclear receptors. A reporter assay was performed to study the potential effects of AR-TR4 heterodimer formation on transactivation. Full-length AR and TR4 in eukaryotic expression vectors (pSG5AR and pCMXTR4) were co-transfected with a CAT reporter containing a TR4-response element (DR4-TK-CAT). More specifically, reporter plasmids (DR4-CAT and CNTFR-15-LUC) (500 ng) were co-transfected with pCMX-TR4 and increasing amounts of pCMV-AR (200, 600 and 1200 ng), pSG5GR (1200 ng) or pSG5PR (1200 ng) using the SuperFect transfection kit. It was found that the CAT activity induced by pCMXTR4 could be repressed significantly in a dose-dependent manner by co-transfection of pSG5AR in the absence or presence of DHT. The repression of TR4 transactivation was AR specific, as other activated steroid receptors such as GR or PR had no suppressive effects. Similar effects were observed when DR4-TK-CAT receptor was replaced with D R1-CNTFR-15-LUC, another response element.

USE - The invention is useful in the control or treatment of diseases or clinical conditions such as hepatitis, hepatoma and hair loss that may relate to TR4 transactivation activity. It is also useful in the treatment of ER-related diseases. In general, modulating nuclear receptor transactivating activity has proved successful in treating diseases that are related to such nuclear transactivating activity. For example, certain types of breast cancer can be controlled by blocking the estrogen receptor transactivation using the antiestrogen tamoxifen.

ADVANTAGE - Understanding how nuclear receptor activity such as that of ***androgen*** receptor, estrogen receptor, TR4 and TR2 is regulated and how these receptors interact with each other will advance the understanding of many human diseases and clinical conditions. Consequently, new treatment options, new drug screening methods and new diagnostic tools will emerge. ***Androgen*** receptor (AR) and TR4 receptor heterodimerize with each other, as do estrogen receptor (ER) and ***TR2*** ***orphan*** ***receptor*** . Such heterodimer formation represses the transactivation activity of both receptors of each heterodimer. This allows TR4-related diseases to be controlled or cured through modulating AR levels, as well as drugs to be screened for TR4-related diseases, by testing their effects on AR level. Similarly the invention makes it possible to screen for drugs for ER-related diseases by testing a compound's effect on TR2 level. It was also found that the RXR receptor can also suppress transactivation of the AR receptor through co-suppression by an allied nuclear receptor.

Dwg.0/10

L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:569604 CAPLUS

DOCUMENT NUMBER: 133:265153

TITLE: The p53/retinoblastoma-mediated repression of testicular orphan receptor-2 in the rhesus monkey with cryptorchidism

AUTHOR(S): Mu, Xiao-Min; Liu, Yi-Xun; Collins, Loretta L.; Kim,

Eungseok; Chang, Chawnshang
CORPORATE SOURCE: Institute of Zoology, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China
SOURCE: Journal of Biological Chemistry (2000), 275(31), 23877-23883
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Whereas the linkage of infertility to cryptorchidism, the failure of the testis to descend into the scrotum at birth, has been well documented, the detailed mol. mechanism remains unclear. Here we report that the testicular orphan receptor-2 (TR2) expression, which modulates many signal pathways, was completely repressed in the surgery-induced cryptorchidism of the rhesus monkey. Further studies link TR2 repression to the induction of p53 and results suggest that induced p53 could repress TR2 expression via the p53.fwdarw.p21.fwdarw.CDK.fwdarw.Rb.fwdarw.E2F signal pathway. In return, TR2 could also control the expression of p53 and Rb through the regulation of human papillomavirus 16 E6/E7 genes. Together, our data suggest a feedback control mechanism between TR2 and p53/Rb tumor suppressors, which might play important roles in male infertility assocd. with cryptorchidism.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:375385 SCISEARCH
THE GENUINE ARTICLE: 313AW
TITLE: Identification of an essential cis-acting element (TR2-PACE) in the 5' promoter of human ***TR2*** ***orphan*** ***receptor*** gene
AUTHOR: Lin D L; Chang C S (Reprint)
CORPORATE SOURCE: UNIV ROCHESTER, MED CTR, DEPT PATHOL, GEORGE WHIPPLE LAB CANC RES, 601 ELMWOOD AVE, BOX 626, ROCHESTER, NY 14642 (Reprint); UNIV ROCHESTER, MED CTR, DEPT PATHOL, GEORGE WHIPPLE LAB CANC RES, ROCHESTER, NY 14642; UNIV ROCHESTER, DEPT UROL, ROCHESTER, NY 14642; UNIV ROCHESTER, DEPT RADIAT ONCOL, ROCHESTER, NY 14642; UNIV ROCHESTER, CTR CANC, ROCHESTER, NY 14642
COUNTRY OF AUTHOR: USA
SOURCE: ENDOCRINE, (FEB 2000) Vol. 12, No. 1, pp. 89-97. Publisher: HUMANA PRESS INC, 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512. ISSN: 0969-711X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The human ***TR2*** ***orphan*** ***receptor*** (***TR2***) is a member of the steroid/thyroid hormone receptor superfamily, It has been shown to be expressed in a wide variety of tissues during development. Using deletion mutation analyses and transient transfection CAT assays, we demonstrated here that a DNA fragment of 103 bp, with a sequence from +65 to -38, containing an initiator is capable of serving as a core promoter to initiate basal level ***transcription*** ; further extending of this core promoter sequence up to -441 maximizes the reporter gene expression. Within this positive regulatory region (-441/+65), we were able to narrow the regulation-responsible sequence down to a small 64-bp (-263/-201) DNA fragment named the TR2 promoter activating cis-element (TR2-PACE). Further deletion mutagenesis and shifting of the insert position followed by reporter assays demonstrated that this TR2-PACE is essential for high-level induction of a heterologous core promoter's activity in a position-dependent nature. In addition, orientation tests indicated that the sense, but not antisense orientation increased the TR2 core promoter activity. Moreover, electrophoresis mobility shift assays and Southwestern analyses suggested that TR2-PACE may interact with un known specific nuclear proteins for its enhancer activity. Together, our data suggest that TR2-PACE is a position-dependent and, in the case of TR2 core promoter (TATA-less), an orientation-dependent cis-activating element required for maximal expression of the TR2 gene.

L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:529246 CAPLUS
DOCUMENT NUMBER: 131:168353

TITLE: Identification of loci involved in accelerated wound healing and the development of new wound healing promoters
INVENTOR(S): Heber-Katz, Ellen
PATENT ASSIGNEE(S): The Wistar Institute, USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941364	A2	19990819	WO 1999-US2962	19990212
WO 9941364	A3	19991223		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319700	AA	19990819	CA 1999-2319700	19990212
AU 9926720	A1	19990830	AU 1999-26720	19990212
EP 1053309	A1	20001122	EP 1999-906924	19990212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002503460	T2	20020205	JP 2000-531545	19990212
US 2003037345	A1	20030220	US 1999-249155	19990212
US 6538173	B2	20030325		
US 2003229911	A1	20031211	US 2002-314322	20021209

PRIORITY APPLN. INFO.:
US 1998-74737P A2 19980213
US 1998-97937P A2 19980826
US 1998-102051P A2 19980928
US 1999-249155 A3 19990212
WO 1999-US2962 W 19990212

AB Genes that quant. improve the efficiency and effectiveness of wound healing in mice are identified. Wound healing is assayed by measuring the time taken for a 2 mm hole punched into the ear to heal. The genes or gene products may be useful in the development of new wound healing promoters, including agents for treatment of central and peripheral nerve wounds. Wound healing in the rapidly healing mouse line MRL was studied. In comparison to the C57BL/6 line, the MRL mice showed more extensive vascularization around wounds with rapid development of sebaceous glands and hair follicles and the unexpected appearance of adipocytes. These mice also showed improved healing of damage to the optic and sciatic nerve after crushing, and of the spinal cord after complete transection. Using the difference in wound healing behavior of the two lines, genetic polymorphisms assocd. with QTLs affecting wound healing were identified. The accelerated healing of the MRL line was lost with aging, and this appeared to be as a result of T-cell actions. Macrophages from the MRL accelerated wound healing in control mice.

L8 ANSWER 8 OF 11 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999094280 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9879671
TITLE: Thyroid hormone direct repeat 4 response element is a positive regulatory element for the human ***TR2*** ***orphan*** ***receptor*** , a member of steroid receptor superfamily.
AUTHOR: Chang C; Pan H J
CORPORATE SOURCE: Department of Pathology, University of Rochester, NY 14642, USA.
SOURCE: Molecular and cellular biochemistry, (1998 Dec) 189 (1-2) 195-200.
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990402
Last Updated on STN: 19990402
Entered Medline: 19990323

AB We demonstrate that ***TR2*** ***orphan*** ***receptor*** (***TR2***) may induce transactivation activities via an AGGTCA-like-direct-repeat-4 consensus thyroid hormone response element (DR4-TRE) system. TR2 showed a slightly greater binding affinity than thyroid hormone receptor alpha1 (TR alpha1)/retinoid X receptor alpha (RXR alpha) heterodimer with Kds 0.5 nM and 2.3 nM, respectively. These ***receptors*** , ***TR2*** and TR alpha1/RXR alpha heterodimer, competed with each other on binding to limited amounts of DR4-TRE. TR2 canceled the suppression effect of unliganded-TR alpha1 on CAT reporter activity in a dose-dependent fashion. Estrogen receptor (ER) and 2P2 (a mutated TR2 with P box sequence of ***androgen*** receptor) failed not only to bind to DR4-TRE but also to recover this inhibitory effect of unliganded TRalpha1. However, when T3 was supplemented, estradiol-ER competed for a full CAT activity while TR2 showed an additive effect on the ***transcriptional*** activation. These results indicate that DNA binding is essential for TR2 to take action and fully functional liganded TR alpha1 may rely on common factors shared with ER but not TR2.

L8 ANSWER 9 OF 11 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 96215345 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8626614
TITLE: Suppression of the human erythropoietin gene expression by the ***TR2*** ***orphan*** ***receptor*** , a member of the steroid receptor superfamily.
AUTHOR: Lee H J; Young W J; Shih C Y; Chang C
CORPORATE SOURCE: Endocrinology-Reproductive Physiology Program, Comprehensive Cancer Center, University of Wisconsin, Madison, Wisconsin 53792, USA.
CONTRACT NUMBER: CA55639 (NCI)
DK47258 (NIDDK)
SOURCE: Journal of biological chemistry, (1996 Apr 26) 271 (17) 10405-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19970203
Entered Medline: 19960621
AB A DNA response element, TR2RE-EPO (5'-TCTGACCTCTCGACCTAC-3') has been identified in the 3-minimal hypoxia-inducible enhancer of the human erythropoietin gene for the ***TR2*** ***orphan*** ***receptor*** , an ***androgen*** -repressed ***transcription*** factor and a member of the steroid/thyroid hormone receptor superfamily. Electrophoretic mobility shift assay showed a specific binding with high affinity (Kd = 0.14 nM) between the ***TR2*** ***orphan*** ***receptor*** and the TR2RE-EPO. Our data further indicated that this specific binding is not due to the homo-dimerization of the ***TR2*** ***orphan*** ***receptor*** . In addition, reporter gene expression using chloramphenicol acetyltransferase assay demonstrated that the ***TR2*** ***orphan*** ***receptor*** may suppress the expression of the chloramphenicol acetyltransferase activities via the TR2RE-EPO in the hypoxic/normoxic human hepatoma HepG2 cells. Finally, our in situ hybridization data also indicated that the ***TR2*** ***orphan*** ***receptor*** and the erythropoietin transcripts can be co-expressed in mouse kidney and liver. Together, our data suggest that the human erythropoietin gene could represent the first human target gene regulated directly by the human ***TR2*** ***orphan*** ***receptor*** .

L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:923168 CAPLUS
DOCUMENT NUMBER: 124:195679
TITLE: Identification of human ***TR2*** ***orphan*** ***receptor*** response element in the ***transcriptional*** initiation site of the simian virus 40 major late promoter. [Erratum to document cited in CA122:257834]
AUTHOR(S): Lee, Han-Jung; Chang, Chawnshang
CORPORATE SOURCE: Dep.Human Oncology and Endocrinology-Reproductive Physiology Prog., Univ. Wisconsin, Madison, WI, 53792, USA
SOURCE: Journal of Biological Chemistry (1995), 270(44), 26721
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Bio

logy
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstr. or the index entries.

L8 ANSWER 11 OF 11 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 95197545 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7890658
TITLE: Identification of human ***TR2*** ***orphan*** ***receptor*** response element in the ***transcriptional*** initiation site of the simian virus 40 major late promoter.
COMMENT: Erratum in: J Biol Chem 1995 Nov 3;270(44):26721
AUTHOR: Lee H J; Chang C
CORPORATE SOURCE: Department of Human Oncology, University of Wisconsin, Madison 53792.
CONTRACT NUMBER: CA 55639 (NCI)
SOURCE: Journal of biological chemistry, (1995 Mar 10) 270 (10) 5434-40.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950427
Last Updated on STN: 19980206
Entered Medline: 19950414
AB A DNA response element (TR2RE-SV40) for the ***TR2*** ***orphan*** ***receptor*** , a member of the steroid-thyroid hormone receptor superfamily, has been identified in the simian virus 40 (SV40) +55 region (nucleotide numbers 368-389, 5'-GTTAAGGTTCGTAGGTCATGGA-3'). Electrophoretic mobility shift assay, using in vitro translated ***TR2*** ***orphan*** ***receptor*** with a molecular mass of 67 kilodaltons, showed a specific binding with high affinity (dissociation constant = 9 nM) for this DNA sequence. DNA-swap experiments using chloramphenicol acetyl-transferase assay demonstrated that ***androgen*** can suppress the ***transcriptional*** activities of SV40 early promoter via the interaction between this TR2RE-SV40 and the chimeric receptor AR/TR2/AR with the DNA-binding domain of the ***TR2*** ***orphan*** ***receptor*** flanked by the N-terminal and ***androgen*** -binding domains of the ***androgen*** receptor. In addition, this TR2RE-SV40 can function as a repressor to suppress the ***transcriptional*** activities of both SV40 early and late promoters. Together, these data suggest the TR2RE-SV40 may represent the first identified natural DNA response element for the ***TR2*** ***orphan*** ***receptor*** that may function as a repressor for the SV40 gene expression.

=> D HIS

FILE 'MEDLINE, JAPIO, BIOSIS, SCISEARCH, WPIDS, CAPLUS, EMBASE' ENTERED

L1 97 S TR2 ORPHAN RECEPTOR#
L2 235 S RECEPTOR TR2
L3 276 S L1 OR L2
L4 35 S L3 AND ANDROGEN#
L5 24 S L4 AND TRANSCRIPTION?
L6 3 L5 AND DISEASE#
L7 2 DUP REM L6 (1 DUPLICATE REMOVED)
L8 11 DUP REM L5 (13 DUPLICATES REMOVED)

=> DUP REM L4
PROCESSING COMPLETED FOR L4
L9 17 DUP REM L4 (18 DUPLICATES REMOVED)

=> D IBIB ABS L9 1-17

L9 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:275624 CAPLUS
TITLE: Two important nuclear receptor signaling pathways, ***androgen*** receptor and ***tr2*** ***orphan*** ***receptor*** , in regulation of breast cancer growth
AUTHOR(S): Hu, Yueh-Chiang

CORPORATE SOURCE: Univ. of Rochester, Rochester, NY, USA
SOURCE: (2003) 132 pp. Avail.: UMI, Order No. DA3092240 From: Diss. Abstr. Int., B 2003, 64(5), 2038
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L9 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:856090 CAPLUS
DOCUMENT NUMBER: 139:346360
TITLE: Method for obtaining the binding affinities of a peptide library to a protein
INVENTOR(S): Guy, Kip R.; Moore, Jamie M. R.; Geistlinger, Timothy R.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089662	A1	20031030	WO 2003-US11766	20030415
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004005636	A1	20040108	US 2003-414583	20030415

PRIORITY APPLN. INFO.: US 2002-372952P P 20020415
OTHER SOURCE(S): MARPAT 139:346360
AB The present invention provides a method for measuring the binding of a peptide library to a target protein, both in the presence and absence of a ligand, or other activation modifier. The peptide library is chosen from known binding partners of the target protein, or members of the family to which it belongs. The members of the peptide library include a conserved interaction motif that permits them to bind to the target protein or its family. Individual peptides from the peptide library and the target protein are contacted with one another and a binding affinity measured. The binding affinities across the library are treated as a 'fingerprint'. The method is preferably applied to a library of co-regulatory peptides that bind to a nuclear hormone receptor. The present invention further comprises the peptide library, and a compn. comprising a member of the peptide library in contact with the target protein.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1007725 CAPLUS
DOCUMENT NUMBER: 140:53957
TITLE: Compositions and methods related to interactions between ***androgen*** receptor, estrogen receptor, and testicular orphan nuclear receptors
INVENTOR(S): Chang, Chawnshang
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of U.S. Ser. No. 711,585.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003235860	A1	20031225	US 2003-366811	20030213

PRIORITY APPLN. INFO.: US 1999-165300P P 19991112
US 2000-711585 A2 20001113
AB Disclosed are compns. and methods related to TR2 (testicular orphan

nuclear receptor 2), TR4 (testicular orphan nuclear receptor 4), ***androgen*** receptor, and estrogen receptor and the interactions between these proteins. Specifically claimed are compns. comprising a fragment of TR2, wherein the compn. interacts with ER, such that ER transcriptional activity is decreased. Methods of identifying an inhibitor of an interaction between ER and TR2 and of identifying inhibitors of ER transcription activity are also claimed. Addnl. claimed are methods of inhibiting TR4 transcription activity comprising administering a compn. that binds TR4, wherein the compn. is AR, AR fragment, AR variant, a mol. that competitively competes with TR4 for AR binding, or a combination thereof. A method of identifying an inhibitor of an interaction between AR and TR4 is also claimed.

L9 ANSWER 4 OF 17 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003411022 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12949936
TITLE: ***TR2*** ***orphan*** ***receptor*** functions as negative modulator for ***androgen*** receptor in prostate cancer cells PC-3.
AUTHOR: Mu Xiaomin; Chang Chawnshang
CORPORATE SOURCE: Department of Pathology, George Whipple Laboratory for Cancer Research, Urology, Radiation Oncology, New York, NY, USA.
CONTRACT NUMBER: DK47258 (NIDDK)
DK63212 (NIDDK)
SOURCE: Prostate, (2003 Oct 1) 57 (2) 129-33.
Journal code: 8101368. ISSN: 0270-4137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030903
Last Updated on STN: 20031029
Entered Medline: 20031028
AB BACKGROUND: Both ***androgen*** receptor (AR) and orphan ***receptor*** ***TR2*** (TR2) belong to the steroid nuclear receptor superfamily and are expressed in prostate cancer tissue and cell lines. AR has been known to be involved in prostate proliferation and prostate cancer progression. AR binds to ***androgen*** response elements and regulates target gene expression via a mechanism involving coregulators. However, the function of TR2 in prostate and prostate cancer and the relationship between TR2 and AR in the prostate cancer is unclear. METHODS: Transient transfection and CAT reporter gene assays were employed to assess AR-mediated transactivation. The expression level of prostate specific antigen (PSA) was measured by Northern blot analysis. The interaction between AR and TR2 was assessed by glutathione-S-transferase (GST) pull-down assay and mammalian two-hybrid system assay. RESULTS: Orphan nuclear ***receptor*** ***TR2*** suppressed ***androgen*** -mediated transactivation in prostate cancer PC-3 cells, and over-expression of TR2 suppressed PSA expression. The suppression of AR mediated transactivation by TR2 is not due to competition for the limited coregulator availability by these two receptors, but possibly through the interaction between TR2 and AR nuclear receptors. CONCLUSIONS: TR2 may function as a negative modulator to suppress AR function in prostate cancer. Further studies on how to control TR2 function may result in the ability to modulate AR function in prostate cancer.

L9 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:668573 CAPLUS
DOCUMENT NUMBER: 140:299252
TITLE: Interaction of nuclear receptor zinc finger DNA binding domains with histone deacetylase
AUTHOR(S): Franco, Peter J.; Li, Guangjin; Wei, Li-Na
CORPORATE SOURCE: Department of Pharmacology, University of Minnesota Medical School, Minneapolis, MN, 55455, USA
SOURCE: Molecular and Cellular Endocrinology (2003), 206(1-2), 1-12
CODEN: MCEND6; ISSN: 0303-7207
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A direct interaction between the nuclear ***receptor*** ***TR2*** and histone deacetylases (HDACs) 3 and 4 is mediated by the DNA binding domain (DBD) of TR2. To test if this interaction is common to members of

the nuclear receptor family, the Cys2-Cys2 type zinc finger (ZF) DBDs were subcloned from several nuclear receptors (mRAR.alpha., mRXR.beta., mTR2, mTR4, RAR, mPPAR.delta., and mPPAR.gamma.2). Using GST pull-downs, both HDACs 3 and 4 were found to interact directly with the core DBD from each receptor. The three-dimensional structure of the ZF domains was essential for this interaction as disruption by zinc chelation precluded interaction with HDACs. The results suggest that the ZFs of nuclear receptors provide a general interaction interface for HDACs 3 and 4. Functional significance of this interaction was demonstrated using ChIP assays where a truncated TR2 protein (lacking the LBD) recruited HDACs 3 and 4 to the target DNA causing demonstrable histone deacetylation. GST pull-downs and mammalian two-hybrid interaction tests were then used to define the interaction domains of HDAC3 with TR2. Both the N- and C-terminal portions of HDAC3 showed interaction with the TR2 DBD. Thus, multiple domains of HDAC3 form the interaction surface for the DBD of nuclear receptors.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:775118 SCISEARCH
THE GENUINE ARTICLE: 592WD
TITLE: Suppression of estrogen receptor-mediated transcription and cell growth by interaction with ***TR2*** ***orphan*** ***receptor***
AUTHOR: Hu Y C; Shyr C R; Che W Y; Mu X M; Kim E; Chang C (Reprint)
CORPORATE SOURCE: Univ Rochester, Med Ctr, George Whipple Lab Canc Res, Dept Pathol, 601 Elmwood Ave, Box 626, Rochester, NY 14642 USA (Reprint); Univ Rochester, Med Ctr, George Whipple Lab Canc Res, Dept Pathol, Rochester, NY 14642 USA; Univ Rochester, Med Ctr, George Whipple Lab Canc Res, Dept Urol, Rochester, NY 14642 USA; Univ Rochester, Med Ctr, Ctr Canc, Rochester, NY 14642 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (13 SEP 2002) Vol. 277, No. 37, pp. 33571-33579.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 62
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The transcriptional activity of the estrogen receptor (ER) is known to be highly modulated by the character and amount of coregulator proteins present in the cells. ***TR2*** ***orphan*** ***receptor*** (***TR2***), a member of the nuclear receptor superfamily without identified ligands, is found to be expressed in the breast cancer cell lines and to function as a repressor to suppress ER-mediated transcriptional activity. Utilizing an interaction blocker, ER-6 (amino acids 312-340), responsible for TR2 interaction, the suppression of ER by TR2 could be reversed, suggesting that this suppression is conferred by the direct protein-protein interaction. Administration of antisense TR2, resulting in an enhancement of ER transcriptional activity in MCF7 cells, indicates that endogenous TR2 normally suppresses ER-mediated signaling. To gain insights into the molecular mechanism by which TR2 suppresses ER, we found that TR2 could interrupt ER DNA binding via formation of an ER-TR2 heterodimer that disrupted the ER homodimerization. The suppression of ER transcription by TR2 consequently caused the inhibition of estrogen-induced cell growth and G(1)/S transition in estrogen-dependent breast cancer cells. Taken together in addition to the potential roles in spermatogenesis and neurogenesis, our data provide a novel biological function of TR2 that may exert an important repressor in regulating ER activity in mammary glands.

L9 ANSWER 7 OF 17 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 2
ACCESSION NUMBER: 2001-381186 [40] WPIDS
DOC. NO. NON-CPI: N2001-279520
DOC. NO. CPI: C2001-116707
TITLE: Method for screening compound, for use in treatment of ***androgen*** - and estrogen-related diseases, comprises testing compound to determine its effects on nuclear receptor-mediated transcriptional activity.
DERWENT CLASS: B04 S03
INVENTOR(S): CHANG, C
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER; (CHAN-I) CHANG C

COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001035101	A2	20010517	(200140)*	EN	37
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001017639	A	20010606	(200152)		
US 2003235860	A1	20031225	(200408)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001035101	A2	WO 2000-US31189	20001113
AU 2001017639	A	AU 2001-17639	20001113
US 2003235860	A1 Provisional	US 1999-165300P	19991112
	CIP of	US 2000-711585	20001113
		US 2003-366811	20030213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001017639	A Based on	WO 2001035101

PRIORITY APPLN. INFO: US 1999-165300P 19991112; US 2000-711585 20001113; US 2003-366811 20030213

AN 2001-381186 [40] WPIDS

AB WO 200135101 A UPAB: 20010719

NOVELTY - A method for screening a compound for use in the treatment of ***androgen*** -related diseases comprises testing the compound to determine its effects on nuclear receptor-mediated transcriptional activity and observing the effect of the compound on the level of ***androgen*** receptor-initiated transcription in the test.

DETAILED DESCRIPTION - A method for screening a compound for use in the treatment of ***androgen*** -related diseases comprises:

(a) testing the compound to determine its effects on nuclear receptor-mediated transcriptional activity, the activity being mediated by a nuclear receptor selected from ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor; and

(b) observing the effect of the compound on the level of ***androgen*** receptor-initiated transcription in the test.

INDEPENDENT CLAIMS are also included for:

(1) a method for screening a compound for use in treatment of estrogen-related diseases comprising:

(a) testing the compound to determine its effects on nuclear receptor-mediated transcriptional activity, the activity being mediated by a nuclear receptor selected from ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor; and

(b) observing the effect of the compound on the level of estrogen receptor-initiated transcription in the test; and

(2) a method for modulating the sensitivity of a cell to a sex hormone comprising the step of stimulating in the cell the abundance (sic) of a nuclear receptor selected from the groups consisting of ***TR2*** ***orphan*** ***receptor*** , the TR4 orphan receptor and the RXR receptor

(3) a method for modulating the ***androgen*** receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate ***TR2*** ***orphan*** ***receptor*** level or TR4 orphan receptor level in the cell;

(4) a method for down regulating ***androgen*** receptor-mediated transactivation activity in a cell comprising introducing TR2 receptor orphan ligand binding domain or TR4 orphan receptor ligand binding domain into the cell;

(5) a method for modulating estrogen receptor-mediated transactivation activity in a cell comprising treating the cell with a compound that can modulate ***TR2*** ***orphan*** ***receptor*** level or TR4 orphan receptor level in the cell;

(6) a method for down regulating ***TR2*** ***orphan*** ***receptor*** -mediated transactivation activity in a cell by

introducing estrogen receptor ligand binding domain into the cell;
(7) a method for screening a compound for treating ***androgen*** receptor-related diseases by exposing cells to the compound and determining the effect of the compound on TR2 or TR4 orphan receptor signaling pathway in the cells; and
(8) a method for screening a compound for treating estrogen receptor-related diseases by exposing cells to the compound and determining the effect of the compound on ***TR2*** ***orphan*** ***receptor*** signaling pathway in those cells.
ACTIVITY - Cytotoxic.
MECHANISM OF ACTION - Suppressor of transactivation activity of nuclear receptors. A reporter assay was performed to study the potential effects of AR-TR4 heterodimer formation on transactivation. Full-length AR and TR4 in eukaryotic expression vectors (pSG5AR and pCMXTR4) were co-transfected with a CAT reporter containing a TR4-response element (DR4-TK-CAT). More specifically, reporter plasmids (DR4-CAT and CNTFR-15-LUC) (500 ng) were co-transfected with pCMX-TR4 and increasing amounts of pCMV-AR (200, 600 and 1200 ng), pSG5GR (1200 ng) or pSG5PR (1200 ng) using the SuperFect transfection kit. It was found that the CAT activity induced by pCMXTR4 could be repressed significantly in a dose-dependent manner by co-transfection of pSG5AR in the absence or presence of DHT. The repression of TR4 transactivation was AR specific, as other activated steroid receptors such as GR or PR had no suppressive effects. Similar effects were observed when DR4-TK-CAT receptor was replaced with D R1-CNTFR-15-LUC, another response element.
USE - The invention is useful in the control or treatment of diseases or clinical conditions such as hepatitis, hepatoma and hair loss that may relate to TR4 transactivation activity. It is also useful in the treatment of ER-related diseases. In general, modulating nuclear receptor transactivating activity has proved successful in treating diseases that are related to such nuclear transactivating activity. For example, certain types of breast cancer can be controlled by blocking the estrogen receptor transactivation using the antiestrogen tamoxifen.
ADVANTAGE - Understanding how nuclear receptor activity such as that of ***androgen*** receptor, estrogen receptor, TR4 and TR2 is regulated and how these receptors interact with each other will advance the understanding of many human diseases and clinical conditions. Consequently, new treatment options, new drug screening methods and new diagnostic tools will emerge. ***Androgen*** receptor (AR) and TR4 receptor heterodimerize with each other, as do estrogen receptor (ER) and ***TR2*** ***orphan*** ***receptor*** . Such heterodimer formation represses the transactivation activity of both receptors of each heterodimer. This allows TR4-related diseases to be controlled or cured through modulating AR levels, as well as drugs to be screened for TR4-related diseases, by testing their effects on AR level. Similarly the invention makes it possible to screen for drugs for ER-related diseases by testing a compound's effect on TR2 level. It was also found that the RXR receptor can also suppress transactivation of the AR receptor through co-suppression by an allied nuclear receptor.
Dwg.0/10

L9 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:569604 CAPLUS
DOCUMENT NUMBER: 133:265153
TITLE: The p53/retinoblastoma-mediated repression of testicular orphan receptor-2 in the rhesus monkey with cryptorchidism
AUTHOR(S): Mu, Xiao-Min; Liu, Yi-Xun; Collins, Loretta L.; Kim, Eungseok; Chang, Chawnshang
CORPORATE SOURCE: Institute of Zoology, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China
SOURCE: Journal of Biological Chemistry (2000), 275(31), 23877-23883
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Whereas the linkage of infertility to cryptorchidism, the failure of the testis to descend into the scrotum at birth, has been well documented, the detailed mol. mechanism remains unclear. Here we report that the testicular orphan receptor-2 (TR2) expression, which modulates many signal pathways, was completely repressed in the surgery-induced cryptorchidism of the rhesus monkey. Further studies link TR2 repression to the induction of p53 and results suggest that induced p53 could repress TR2 expression via the p53.fwdarw.p21.fwdarw.CDK.fwdarw.Rb.fwdarw.E2F signal pathway. In return, TR2 could also control the expression of p53 and Rb

through the regulation of human papillomavirus 16 E6/E7 genes. Together, our data suggest a feedback control mechanism between TR2 and p53/Rb tumor suppressors, which might play important roles in male infertility assocd. with cryptorchidism.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:375385 SCISEARCH
THE GENUINE ARTICLE: 313AW
TITLE: Identification of an essential cis-acting element (TR2-PACE) in the 5' promoter of human ***TR2*** ***orphan*** ***receptor*** gene
AUTHOR: Lin D L; Chang C S (Reprint)
CORPORATE SOURCE: UNIV ROCHESTER, MED CTR, DEPT PATHOL, GEORGE WHIPPLE LAB CANC RES, 601 ELMWOOD AVE, BOX 626, ROCHESTER, NY 14642 (Reprint); UNIV ROCHESTER, MED CTR, DEPT PATHOL, GEORGE WHIPPLE LAB CANC RES, ROCHESTER, NY 14642; UNIV ROCHESTER, DEPT UROL, ROCHESTER, NY 14642; UNIV ROCHESTER, DEPT RADIAT ONCOL, ROCHESTER, NY 14642; UNIV ROCHESTER, CTR CANC, ROCHESTER, NY 14642
COUNTRY OF AUTHOR: USA
SOURCE: ENDOCRINE, (FEB 2000) Vol. 12, No. 1, pp. 89-97. Publisher: HUMANA PRESS INC, 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512. ISSN: 0969-711X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The human ***TR2*** ***orphan*** ***receptor*** (***TR2***) is a member of the steroid/thyroid hormone receptor superfamily, It has been shown to be expressed in a wide variety of tissues during development. Using deletion mutation analyses and transient transfection CAT assays, we demonstrated here that a DNA fragment of 103 bp, with a sequence from +65 to -38, containing an initiator is capable of serving as a core promoter to initiate basal level transcription; further extending of this core promoter sequence up to -441 maximizes the reporter gene expression. Within this positive regulatory region (-441/+65), we were able to narrow the regulation-responsible sequence down to a small 64-bp (-263/-201) DNA fragment named the TR2 promoter activating cis-element (TR2-PACE). Further deletion mutagenesis and shifting of the insert position followed by reporter assays demonstrated that this TR2-PACE is essential for high-level induction of a heterologous core promoter's activity in a position-dependent nature. In addition, orientation tests indicated that the sense, but not antisense orientation increased the TR2 core promoter activity. Moreover, electrophoresis mobility shift assays and Southwestern analyses suggested that TR2-PACE may interact with un known specific nuclear proteins for its enhancer activity. Together, our data suggest that TR2-PACE is a position-dependent and, in the case of TR2 core promoter (TATA-less), an orientation-dependent cis-activating element required for maximal expression of the TR2 gene.

L9 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:529246 CAPLUS
DOCUMENT NUMBER: 131:168353
TITLE: Identification of loci involved in accelerated wound healing and the development of new wound healing promoters
INVENTOR(S): Heber-Katz, Ellen
PATENT ASSIGNEE(S): The Wistar Institute, USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941364	A2	19990819	WO 1999-US2962	19990212
WO 9941364	A3	19991223		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,

MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2319700	AA	19990819	CA 1999-2319700	19990212	
AU 9926720	A1	19990830	AU 1999-26720	19990212	
EP 1053309	A1	20001122	EP 1999-906924	19990212	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002503460	T2	20020205	JP 2000-531545	19990212	
US 2003037345	A1	20030220	US 1999-249155	19990212	
US 6538173	B2	20030325			
US 2003229911	A1	20031211	US 2002-314322	20021209	

PRIORITY APPLN. INFO.:
US 1998-74737P A2 19980213
US 1998-97937P A2 19980826
US 1998-102051P A2 19980928
US 1999-249155 A3 19990212
WO 1999-US2962 W 19990212

AB Genes that quant. improve the efficiency and effectiveness of wound healing in mice are identified. Wound healing is assayed by measuring the time taken for a 2 mm hole punched into the ear to heal. The genes or gene products may be useful in the development of new wound healing promoters, including agents for treatment of central and peripheral nerve wounds. Wound healing in the rapidly healing mouse line MRL was studied. In comparison to the C57BL/6 line, the MRL mice showed more extensive vascularization around wounds with rapid development of sebaceous glands and hair follicles and the unexpected appearance of adipocytes. These mice also showed improved healing of damage to the optic and sciatic nerve after crushing, and of the spinal cord after complete transection. Using the difference in wound healing behavior of the two lines, genetic polymorphisms assocd. with QTLs affecting wound healing were identified. The accelerated healing of the MRL line was lost with aging, and this appeared to be as a result of T-cell actions. Macrophages from the MRL accelerated wound healing in control mice.

L9 ANSWER 11 OF 17 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999094280 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9879671
TITLE: Thyroid hormone direct repeat 4 response element is a positive regulatory element for the human ***TR2*** ***orphan*** ***receptor*** , a member of steroid receptor superfamily.
AUTHOR: Chang C; Pan H J
CORPORATE SOURCE: Department of Pathology, University of Rochester, NY 14642, USA.
SOURCE: Molecular and cellular biochemistry, (1998 Dec) 189 (1-2) 195-200.
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990402
Last Updated on STN: 19990402
Entered Medline: 19990323

AB We demonstrate that ***TR2*** ***orphan*** ***receptor*** (***TR2***) may induce transactivation activities via an AGGTCA-like-direct-repeat-4 consensus thyroid hormone response element (DR4-TRE) system. TR2 showed a slightly greater binding affinity than thyroid hormone receptor alpha1 (TR alpha1)/retinoid X receptor alpha (RXR alpha) heterodimer with Kds 0.5 nM and 2.3 nM, respectively. These ***receptors*** , ***TR2*** and TR alpha1/RXR alpha heterodimer, competed with each other on binding to limited amounts of DR4-TRE. TR2 canceled the suppression effect of unliganded-TR alpha1 on CAT reporter activity in a dose-dependent fashion. Estrogen receptor (ER) and 2P2 (a mutated TR2 with P box sequence of ***androgen*** receptor) failed not only to bind to DR4-TRE but also to recover this inhibitory effect of unliganded TRalpha1. However, when T3 was supplemented, estradiol-ER competed for a full CAT activity while TR2 showed an additive effect on the transcriptional activation. These results indicate that DNA binding is essential for TR2 to take action and fully functional liganded TR alpha1 may rely on common factors shared with ER but not TR2.

L9 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:313338 CAPLUS
DOCUMENT NUMBER: 126:288219
TITLE: The developmental expression patterns of the ***androgen*** , TR2, and TR4 receptors in relation to their roles in the target organs (steroid hormones)
AUTHOR(S): Young, Win-Jing
CORPORATE SOURCE: Univ. of Wisconsin, Madison, WI, USA
SOURCE: (1996) 173 pp. Avail.: Univ. Microfilms Int., Order No. DA9708699
From: Diss. Abstr. Int., B 1997, 57(11), 6779
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L9 ANSWER 13 OF 17 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 96215345 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8626614
TITLE: Suppression of the human erythropoietin gene expression by the ***TR2*** ***orphan*** ***receptor*** , a member of the steroid receptor superfamily.
AUTHOR: Lee H J; Young W J; Shih C Y; Chang C
CORPORATE SOURCE: Endocrinology-Reproductive Physiology Program, Comprehensive Cancer Center, University of Wisconsin, Madison, Wisconsin 53792, USA.
CONTRACT NUMBER: CA55639 (NCI)
DK47258 (NIDDK)
SOURCE: Journal of biological chemistry, (1996 Apr 26) 271 (17) 10405-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19970203
Entered Medline: 19960621
AB A DNA response element, TR2RE-EPO (5'-TCTGACCTCTCGACCTAC-3') has been identified in the 3-minimal hypoxia-inducible enhancer of the human erythropoietin gene for the ***TR2*** ***orphan*** ***receptor*** , an ***androgen*** -repressed transcription factor and a member of the steroid/thyroid hormone receptor superfamily. Electrophoretic mobility shift assay showed a specific binding with high affinity (Kd = 0.14 nM) between the ***TR2*** ***orphan*** ***receptor*** and the TR2RE-EPO. Our data further indicated that this specific binding is not due to the homo-dimerization of the ***TR2*** ***orphan*** ***receptor*** . In addition, reporter gene expression using chloramphenicol acetyltransferase assay demonstrated that the ***TR2*** ***orphan*** ***receptor*** may suppress the expression of the chloramphenicol acetyltransferase activities via the TR2RE-EPO in the hypoxic/normoxic human hepatoma HepG2 cells. Finally, our in situ hybridization data also indicated that the ***TR2*** ***orphan*** ***receptor*** and the erythropoietin transcripts can be co-expressed in mouse kidney and liver. Together, our data suggest that the human erythropoietin gene could represent the first human target gene regulated directly by the human ***TR2*** ***orphan*** ***receptor*** .

L9 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:923168 CAPLUS
DOCUMENT NUMBER: 124:195679
TITLE: Identification of human ***TR2*** ***orphan*** ***receptor*** response element in the transcriptional initiation site of the simian virus 40 major late promoter. [Erratum to document cited in CA122:257834]
AUTHOR(S): Lee, Han-Jung; Chang, Chawnshang
CORPORATE SOURCE: Dep.Human Oncology and Endocrinology-Reproductive Physiology Prog., Univ. Wisconsin, Madison, WI, 53792, USA
SOURCE: Journal of Biological Chemistry (1995), 270(44), 26721
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstr. or the index entries.

L9 ANSWER 15 OF 17 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 95197545 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7890658
TITLE: Identification of human ***TR2*** ***orphan*** ***receptor*** response element in the transcriptional initiation site of the simian virus 40 major late promoter.
COMMENT: Erratum in: J Biol Chem 1995 Nov 3;270(44):26721
AUTHOR: Lee H J; Chang C
CORPORATE SOURCE: Department of Human Oncology, University of Wisconsin, Madison 53792.
CONTRACT NUMBER: CA 55639 (NCI)
SOURCE: Journal of biological chemistry, (1995 Mar 10) 270 (10) 5434-40.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950427
Last Updated on STN: 19980206
Entered Medline: 19950414

AB A DNA response element (TR2RE-SV40) for the ***TR2*** ***orphan*** ***receptor*** , a member of the steroid-thyroid hormone receptor superfamily, has been identified in the simian virus 40 (SV40) +55 region (nucleotide numbers 368-389, 5'-GTTAAGGTTCGTAGGTCATGGA-3'). Electrophoretic mobility shift assay, using in vitro translated ***TR2*** ***orphan*** ***receptor*** with a molecular mass of 67 kilodaltons, showed a specific binding with high affinity (dissociation constant = 9 nM) for this DNA sequence. DNA-swap experiments using chloramphenicol acetyl-transferase assay demonstrated that ***androgen*** can suppress the transcriptional activities of SV40 early promoter via the interaction between this TR2RE-SV40 and the chimeric receptor AR/TR2/AR with the DNA-binding domain of the ***TR2*** ***orphan*** ***receptor*** flanked by the N-terminal and ***androgen*** -binding domains of the ***androgen*** receptor. In addition, this TR2RE-SV40 can function as a repressor to suppress the transcriptional activities of both SV40 early and late promoters. Together, these data suggest the TR2RE-SV40 may represent the first identified natural DNA response element for the ***TR2*** ***orphan*** ***receptor*** that may function as a repressor for the SV40 gene expression.

L9 ANSWER 16 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 6
ACCESSION NUMBER: 95:379879 SCISEARCH
THE GENUINE ARTICLE: QZ873
TITLE: GENE-EXPRESSION OF THE ***ANDROGEN*** REPRESSED RAT ***TR2*** ***ORPHAN*** ***RECEPTOR*** - A MEMBER OF STEROID-RECEPTOR SUPERFAMILY
AUTHOR: IDETA R; YEH S Y; LEE Y F; ADACHI K; TAKEDA H; SU C Y; SALTZMAN A; CHANG C S (Reprint)
CORPORATE SOURCE: UNIV WISCONSIN, DEPT HUMAN ONCOL, MADISON, WI, 53792 (Reprint); UNIV WISCONSIN, DEPT HUMAN ONCOL, MADISON, WI, 53792; UNIV WISCONSIN, PROGRAM ENDOCRINOL & REPROD PHYSIOL, MADISON, WI, 53792; SHISEIDO RES CTR, ADACHI RES LABS, YOKOHAMA, KANAGAWA, JAPAN
COUNTRY OF AUTHOR: USA; JAPAN
SOURCE: ENDOCRINE, (APR 1995) Vol. 3, No. 4, pp. 277-283.
ISSN: 0969-711X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 21

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A full-length rat cDNA clone was obtained from the ***TR2*** ***orphan*** ***receptor*** , a member of the steroid receptor superfamily, using cDNA library screening and 3' RACE-PCR technology. Under these conditions, only the TR2-11 form of the ***TR2*** ***orphan*** ***receptor*** , the major form found in prostate, was identified. The overall amino acid homology between human and rat TR2-11 orphan receptors was near 90% with one amino acid difference in the DNA-binding domain sequence. Northern blot analysis identified multiple forms of the ***TR2*** ***orphan*** ***receptor*** mRNAs expressed in human and rat prostates. ***Androgens*** repressed ***TR2*** ***orphan*** ***receptor*** mRNA levels in human prostate LNCaP cells and rat ventral prostate. Polyclonal anti- ***TR2***

orphan ***receptor*** antibodies raised from a unique ***TR2*** ***orphan*** ***receptor*** 20 amino acid peptide were used to localize the ***TR2*** ***orphan*** ***receptor*** in the nuclei of prostate and epididymis epithelium cells. Together, these data demonstrate that the ***TR2*** ***orphan*** ***receptor*** can be expressed at mRNA and protein levels in the human and rat prostrates and may have some potential function in mediating ***androgen*** action in these tissues.

L9 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:549644 CAPLUS
DOCUMENT NUMBER: 123:307954
TITLE: Gene expression of the ***androgen*** repressed rat ***TR2*** ***orphan*** ***receptor***: a member of steroid receptor superfamily
AUTHOR(S): Ideta, Ritsuro; Yeh, Shuyuan; Lee, ZYifen; Adachi, Kenji; Takeda, Hiroyuki; Su, Chingyuan; Saltzman, Alan; Chang, Chawnshang
CORPORATE SOURCE: Dep. of Human Oncology and Program in Endocrinology and Reprod. Physiol., Univ. of Wisconsin, Madison, WI, 53792, USA
SOURCE: Endocrine (1995), 3(4), 277-83
CODEN: EOCRE5; ISSN: 1355-008X
PUBLISHER: Humana
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A full-length rat cDNA clone was obtained from the ***TR2*** ***orphan*** ***receptor*** , a member of the steroid receptor superfamily, using cDNA library screening and 3' RACE-PCR technol. Under these conditions, only the TR2-11 form of the ***TR2*** ***orphan*** ***receptor*** , the major form found in prostate, was identified. The overall amino acid homol. between human and rat TR2-11 orphan receptors was near 90% with one amino acid difference in the DNA-binding domain sequence. Northern blot anal. identified multiple forms of the ***TR2*** ***orphan*** ***receptor*** mRNAs expressed in human and rat prostates. ***Androgens*** repressed ***TR2*** ***orphan*** ***receptor*** mRNA levels in human prostate LNCaP cells and rat ventral prostate. Polyclonal anti- ***TR2*** ***orphan*** ***receptor*** antib.omega.dies raised from a unique ***TR2*** ***orphan*** ***receptor*** 20 amino acid peptide were used to localize the ***TR2*** ***orphan*** ***receptor*** in the nuclei of prostate and epididymis epithelium cells. Thus, the ***TR2*** ***orphan*** ***receptor*** can be expressed at mRNA and protein levels in the human and rat prostates and may have some potential function in mediating ***androgen*** action in these tissues.

Refine Search

Search Results -

Term	Documents
"5208263"	1
5208263S	0
"5208263".PN..USPT.	1
(5208263.PN.).USPT.	1

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L4

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Monday, May 03, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=ADJ			
L4	5208263.pn.	1	L4
L3	5677336.pn.	1	L3
L2	5208260.pn.	1	L2
L1	5674703.pn.	1	L1

END OF SEARCH HISTORY

Refine Search

Search Results -

Term	Documents
TR2	12787
TR2S	17
(18 AND TR2).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	6
(L18 AND TR2).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	6

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L19

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Sunday, May 02, 2004 Printable Copy Create Case

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L19	L18 and tr2	6	L19
L18	chang-chawnshang.in.	16	L18
L17	L16 and l4	2	L17
L16	receptor tr2	35	L16
L15	L14 and l4	3	L15
L14	tr2 near10 receptor	81	L14
L13	tr2 near$10 receptor	0	L13
L12	tr2 near $10 receptor	0	L12
L11	tr2 same receptor	127	L11

L10	tr2 with receptor	89	L10
L9	tr2	12792	L9
L8	l1 and l5	2	L8
L7	l1 and l4	2	L7
L6	l1 and l2	2	L6
L5	nuclear same mediated same transcriptional same activity same treatment	31	L5
L4	nuclear same mediated same transcriptional same activity	258	L4
L3	nuclear with mediated with transcriptional with activity	27	L3
L2	androgen	9400	L2
L1	tr2 orphan receptor	4	L1

END OF SEARCH HISTORY